



Received on 10 August, 2014; received in revised form, 21 October, 2014; accepted, 15 December, 2014; published 01 April, 2015

EVALUATION OF BONE MARROW FOR HEMATOLOGICAL ANOMALIES IN INDIAN PEDIATRIC AND ADULT PATIENTS: A SINGLE TERTIARY CARE CENTER STUDY

Ishwar Singh¹, Rohit Jain², G. N. Gupta² and P. K. Goyal^{*1}

Radiation & Cancer Biology Laboratory¹, Department of Zoology, University of Rajasthan, Jaipur, Rajasthan - 302 004, India

Department of Pathology², Santokba Dhurlabhji Memorial Hospital & Research Institute, Jaipur, Rajasthan - 302 015, India

Keywords:

Trepine Biopsy,
Bone Marrow Aspiration,
Hematological Anomalies

Correspondence to Author:

Dr. P. K. Goyal

Professor & Head
Department of Zoology
University of Rajasthan
Jaipur, Rajasthan - 302 004, India

E-mail: pkgoyal2002@gmail.com

ABSTRACT: Bone marrow aspiration can determine the metastatic deposits, degree of cellularity and fibrosis readily. A retrospective analysis of bone marrow aspiration and biopsy, in children and adult patients with hematological anomalies, were performed in 674 cases for different indication of hematological abnormalities from January 2013 to March 2014. Cases were analyzed in detail regarding clinical, hematological examination and family history. The mean age of the patients was 38.03 years ranging from 2 years to 78 years. Among 674 cases, 58.16 percent cases were male and 41.84 percent were female with sex ratio of 1.4:1. The commonest clinical & physical symptoms were pallor (87.5%), followed by weakness & headache (47.9%) and fever (37.9%). The most frequent malignant hematological anomalies in children (99.9%) and adults (50.49%) were acute leukemia, followed by multiple myeloma (17.82%) in adults only. Normoblastic marrow represented highest number of cases both in children (21.43%) and in adults (20.86%) as non-malignant hematological disorder. Bone marrow examination helps to assess the spectrum of hematological disorder in both children & adults within a short span of time. In the present study, males were more affected from hematological disorders than females whereas acute leukemia had the highest occurrence among the malignant hematological disorders in both pediatric and adult patients.

INTRODUCTION: World health organization associated health group reported in 2013, the concentrations of mean hemoglobin were lowest and anemia prevalence was highest in south Asia and central and west Africa. In India, the prevalence of anemia was severe (>35 %) in preschool-age children and pregnant women.¹

Ministry of Health & Family welfare, India reported in 2011 that over 40% of children and 36% of adults and women are undernourished, with the persistent level of malnutrition, which is of great concern.² Bone marrow examination (BME) helps to assess the spectrum of hematological disorders in both children & adults within a short span of time.

Bone marrow was first obtained from living patients for diagnostic purposes during the first decade of the 20th century but it was not until the introduction of sternal aspiration in the late 1920s which became an important diagnostic procedure.³ Bone marrow aspiration can determine the

<p>QUICK RESPONSE CODE</p> 	<p>DOI: 10.13040/IJPSR.0975-8232.6(4).1584-89</p>
<p>Article can be accessed online on: www.ijpsr.com</p>	
<p>DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.6(4).1585-89</p>	

metastatic deposits, degree of cellularity and fibrosis readily. The bone marrow picture may vary depending on the etiology, from normocellular with non specific changes to hypercellular being replaced completely by malignant cells. Clinical, hematological and morphological peripheral blood and bone marrow characteristics reveal diagnostic clues and pathognomonic features of the disease. Bone marrow aspiration (BMA) examination is one of the most frequent and relatively safe invasive procedures. Though an invasive procedure, it can be easily performed even in the presence of thrombocytopenia with little or no risk of bleeding.⁴

Few studies have been performed to evaluate the spectrum of hematological disorders in developing and developed countries; however, none of the study has been performed until now in Rajasthan, the largest state of India.^{5,6} The present study was designed to evaluate the clinical & etiological spectrum, occupation based history and bone marrow findings in children and adults patients with hematological anomalies in this part of Northern region of India.

MATERIALS AND METHODS:

Study participants: A retrospective analysis of bone marrow aspiration and biopsy were performed in 674 cases for different indications of hematological abnormalities from hematology clinics at Santokba Dhurlabhji Memorial Hospital & Research Institute during the period of January 2013 to March 2014. This study was approved by the Departmental Ethics Committee. The written consents were obtained from all the patients for their participation in the study.

Clinical analysis: Clinical profiles of all the patients were analyzed in detail. Family history, physical and clinical examination were recorded. Indications for bone marrow examination included blast or atypical cells in peripheral blood, staging of malignancy, hepatomegaly, lymphadenopathy, fatigue & headache, pancytopenia, splenomegaly, dyspnea on exertion, bleeding, menorrhagia (only in females) etc.

Bone marrow analysis: Bone marrow was aspirated from posterior superior iliac spine by 'BD

Spinal Needle 18GA 3.5IN' and slides were prepared according to the standard procedures.^{3,11} For the assessment of bone marrow cellularity and of iron stores, aspirates were stained with May-Grunwald-Giemsa and Perls' stain, respectively.

The bone marrow trephine biopsy samples (2 cm in length) were taken from the same site by 'Rup's Bone Marrow Biopsy Needle' and stained with Hematoxylin and eosin. Interpretation of biopsy material was done according to the cellularity comparison of the relative proportions of myeloid, erythroid and megakaryocytic cells, other bone elements and reticulin. The overall cases were distributed in two groups as following:

Group A: Pediatric patients with age < 15 years

Group B: Adults patients with age > 15 years

RESULTS: In this study, 674 cases were finally diagnosed with hematological disorders in which 108 (16.02%) cases belonged to children and 566 (83.98%) of adults. Among all the cases, 392 (58.16%) patients were male and 282 (41.84%) were female with sex ratio of 1.4:1. The mean age of the patients was 38.03 years ranging from 2 years to 78 years. Clinical findings are depicted in (Figure 1).

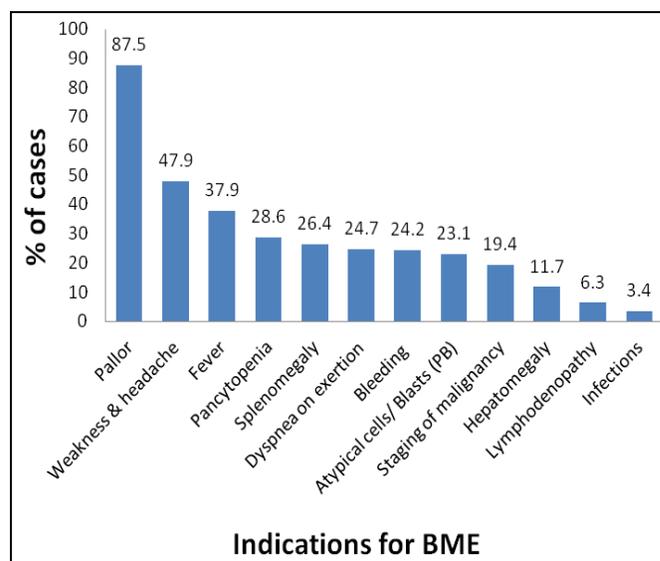


FIGURE 1: DISTRIBUTION OF THE PATIENTS ACCORDING TO INDICATIONS FOR BONE MARROW EXAMINATION.

Most common symptoms were pallor (87.5%), weakness & headache (47.9%) and fever (37.9%). 193 (28.64%) cases presented with pancytopenia and 167 (24.78%) had bleeding from nose, gums and hematuria.

In the final diagnosis, among 125 hematological malignancies, distribution of acute leukemia was the highest in both children (99.9%) and adults (50.49%). Further, in adults, multiple myeloma (MM), chronic lymphoid leukemia (CLL), chronic

myeloid leukemia (CML), metastatic carcinoma and Hodgkins lymphoma were observed in 17.82, 11.88, 8.91, 5.94 and 4.95 percent cases respectively as seen in (Table 1).

TABLE 1: COMPARISON OF HEMATOLOGICAL ANOMALIES IN CHILDREN AND ADULT (MALIGNANT).

Bone marrow findings	No. of Cases		Total
	Children (<15 yrs) (%)	Adult (>15 yrs) (%)	
Acute Myeloid Leukemia	14 (58.33)	44(43.56)	58(46.4)
Multiple Myeloma	0 (0.00)	18(17.82)	18(14.4)
Acute Lymphoblastic Leukemia	10 (41.66)	7(6.93)	17(13.6)
Chronic Lymphoid Leukemia	0(0.00)	12(11.88)	12(9.6)
Chronic Myeloid Leukemia	0(0.00)	9(8.91)	9(7.2)
Metastatic Carcinoma	0(0.00)	6(5.94)	6(4.8)
Hodgkins Lymphoma	0(0.00)	5(4.95)	5(4.0)
Total	24	101	125

Most common malignant hematological anomaly was acute Myeloid leukemia (46.4%) whereas least was Hodgkins lymphoma (4.0%).

Out of 549 non-malignant hematological anomalies, normoblastic marrow was diagnosed in the highest number of cases 115 (20.95%) in which pediatric cases were 18 (21.43%) while adult cases

were 97 (20.86%) in respective group. Other cases of bone marrow abnormalities are shown in (Table 2). Comparative studies regarding sex, mean age and common causes are shown in (Table 3).

TABLE 2: COMPARISON OF HEMATOLOGICAL ANOMALIES IN CHILDREN AND ADULTS (NON-MALIGNANT).

Bone marrow findings	No. of Cases		Total
	Children (<15 yrs) (%)	Adult (>15 yrs) (%)	
Normoblastic marrow	18 (21.43)	97(20.86)	115(20.95)
Megaloblastic marrow	12(14.29)	58(12.47)	70(12.75)
Dimorphic erythroid hyperplasia	5(5.59)	62(13.33)	67(12.20)
Hypoplastic Marrow	9(10.71)	54(11.61)	63(11.48)
Aplastic marrow	11(13.10)	46(9.89)	57(10.38)
Myeloid Hyperplasia	9(10.71)	33(7.10)	42(7.65)
Atypical cells advised IHC (immuno marker)	2(2.38)	36(7.74)	38(6.92)
Dilluted with peripheral blood	8(9.52)	26(5.59)	34(6.19)
MEH	2(2.38)	19(4.09)	21(3.83)
Hypercellular	2(2.38)	18(3.87)	20(3.64)
Suboptimal	2(2.38)	10(2.15)	12(2.19)
Micronormoblastic marrow	4(4.76)	2(0.43)	6(1.09)
Megakaryotic thrombocytopenia	0(00.0)	4(0.86)	4(0.73)
Total	84	465	549

Most common non-malignant hematological anomaly was Normoblastic marrow (20.95%) whereas least was Megakaryotic thrombocytopenia (0.73%).

TABLE 3: COMMON CAUSES OF BLOOD ANOMALIES FINDINGS OF BONE MARROW EXAMINATION IN DIFFERENT STUDIES.

Study	Country	Year	No. of Cases	Sex Ratio	Age Range (yrs)	Mean Age (yrs)	Commonest Diagnosis	Second Most Common Diagnosis
Khan et al ⁷	Pakistan	2008	198	1.53:1	6-14 y	5.35	Aplastic anemia	Idiopathic thrombocytopenic
Saeed et al ⁹	Iraq	2010	117	1.49:1	2-76yr	46.16	Lymphoma	Acute leukemia
Kibria et al ⁵	Bangladesh	2010	177	1.68:1	10-19	27.05	Acute Myeloid	Acute

Jha et al ⁸	Nepal	2013	86	1.26:1	2-80	13	Leukemia Acute leukemia	Lymphoblastic Leukemia Chronic myeloid leukemia
Shastry et al ⁴	India	2012	110	1.03:1	0-90	-	Megaloblastic anemia	Acute myeloid leukemia
Nigam et al ¹⁰	India	2014	345	1.28:1	2-80	-	Megaloblastic anemia	Dimorphic anemia
Present study	India	2014	674	1.4:1	2-78	38.03	Normoblastic	Megaloblastic anemia

Higher sex ratio (1.4:1) was present with 38.03 median age reflecting the higher incidences in males alongwith predominant age group between 3rd and 4th decade.

DISCUSSION: Hematological disorders are the major global public health problem affecting both developing and developed countries with severe consequences for human health as well as socio-economic development.¹ These occur at all stages of the life cycle but are more prevalent in the pregnant women and young children. Anemia is an indicator of both malnutrition and poor health. The most dramatic health effects of anemia, i.e. increased risk of maternal and child mortality, have been well reported by World Health Organization in the 2013 and Ministry of Health & Family Welfare, India.^{1,2}

Bone marrow aspiration and biopsy are the obligatory tools, for the assessment of bone marrow cellularity³, fibrosis, metastatic deposits and architectural patterns of histological diagnostic procedures.⁴ The range of hematological anomalies both in children and adults is vast. Clinico-hematological analysis, bone marrow aspiration & biopsy outcomes provide optimal result in different age groups.

In the present study, sex ratio is 1.4:1 which is higher than previous studies carried out in different parts of India.^{4, 10} and Western Asia.⁸ However, such ratio is found to be lower in comparison to Pakistan⁷, Bangladesh⁵ and Iraq.⁹ Median age in this study was 38.03 years reflecting the predominant age group between 3rd and 4th decade which is higher (13 years) to the study by Jha A⁸ in Nepal whereas lower (46.16 years) to the study by Saeed et al in Iraq.⁹ Pallor was the most common clinical presentation (87.54% cases) which is solely or partly associated with other features and also

noted in previous studies.^{4, 10} Body weakness and headache were the second most common clinical presentation in 47.92% cases. Fever accounted for 37.98 % cases and pancytopenia for 28.64% cases which are comparatively lower than the other studies.¹¹

Overall, acute leukemia was diagnosed in 58 (46.4%) cases out of the total 125 cases of malignant hematological anomalies, 18 (58.33%) pediatric cases out of 24 cases and 44 (43.56%) adults out of 101 cases. Such incidences were higher to other study performed in Iraq.⁹ Multiple myeloma, found in 14.4% adult cases, was also higher than the previous studies.^{4,9} CLL, CML and Metastatic carcinoma were diagnosed in 13.6%, 7.2% and 4.8% cases respectively, in adults only. Hodgkins lymphoma was the least common hematological malignancy in the adults (4.0%). It is primarily a disease of lymphatic system and hence rarely involves the bone marrow.

Normoblastic marrow was diagnosed in 115 (20.95%) of total non-malignant cases of hematological anomalies in the children and adults. Megaloblastic anemia contributed to 12.75% of total cases which is lower (18.4%) than study by Mahajan *et al.*¹⁴ Dimorphic erythroid hyperplasia (12.20%), hypoplastic marrow (11.48%) and aplastic marrow (10.38%) contributed to one third of total cases presented as non-malignant form whereas micronormoblastic marrow was the least (1.09%) found disorder.

In our study, most common diagnosis in nonmalignant group was normoblastic marrow

followed by megaloblastic anemia. Nigam *et al*¹⁰ reported overall 41.81% cases of megaloblastic anemia as unusually high in central India. The findings of present study are similar to others as majority of cases were megaloblastic marrow (12.75%) in comparison to 12.3% reported by Pudasaini *et al*¹¹ in Nepal & 14.6% reported by Khan *et al*⁷ in Pakistan. Furthermore, the commonest causes of hematological abnormalities reported in different studies across the South-West Asian countries^{5, 7, 8} have been aplastic anemia, megaloblastic anemia and acute leukemia. The salient findings of various studies on hematological disorders are summarized in (Table 3), however, they have different geographical locations, nutritional practices and life styles.

In the present study, more than 80% (541) cases belonged to rural, sub-urban region and agricultural backgrounds, with lower socio-economic status and lack of appropriate education, therefore, they had exposure to various risk factors coincidentally and finally faced to haematological abnormalities.

CONCLUSION: Bone marrow examination helps to assess the spectrum of hematological disorder in both children & adult within a short span of time. In the present study, males were more affected from hematological disorders than the females. Acute leukemia as malignant hematological diagnosis whereas normoblastic marrow as non-malignant hematological diagnosis, had the highest occurrence in both pediatric and adult patients. Interestingly, the incidence of multiple myeloma is on rise in our study. Hematological anomalies were dispersed in lower socio-economic strata of the society.

The clinical findings and bone marrow examination provide precious information to help in planning investigations, such as immunophenotyping and cytogenetic studies. In addition, an early recognition of the underlying conditions will certainly have an impact on the mortality and morbidity in vulnerable patients for better prognosis. However, maximum diagnostic yield can be achieved by the clinico-pathological correlation and enormous data analysis. Further, long term follow-up is required to observe the profile, spectrum and prognosis of the hematological diseases.

CONFLICT OF INTEREST: The authors declare that we have no conflict of interest.

ACKNOWLEDGEMENT: The study was supported in part by the University Grants Commission, Government of India, New Delhi. We thank the physicians and patients who provided bone marrow biopsy slides for review.

REFERENCES:

1. Stevens GA, Finucane MM, De-Regil LM, Paciorek CJ. et al: Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. *Lancet Glob Health* 2013; 1:e16–25.
2. Annual report to the people on health. Published by Ministry of Health and Family Welfare, Government of India, Dec. 2011.
3. Gong X, Lu X, Wu X, Xu R, et al. Role of bone marrow imprints in haematological diagnosis: a detailed study of 3781 cases. *Cytopathology* 2012; 23(2):86-95.
4. Shastry SM, Kolte SS. Spectrum of hematological disorders observed in one hundred and ten consecutive bone marrow aspirations and biopsy. *Med. J. Dr. D.Y. Patil Univ.* 2012; 5(2):118-121.
5. Kibria SG, Islam MDU, Chowdhury ASMJ, Ali MY, et al. Prevalence of Hematological Disorder: A Bone Marrow Study Of 177 Cases In A Private Hospital At Faridpur. *Faridpur Med. Coll. J.* 2010; 5(1):11-13.
6. Pandya A, Patel T, Shah N. Comparative Utility of Bone Marrow Aspiration and Bone Marrow Biopsy. *J. Evo. Medi. Dent. Sci.* 2012; 1(6):987-993.
7. Khan A, Aqeel M, Khan TK, Munir A. Pattern of Hematological Diseases In Hospitalized Paediatric Patients Based On Bone Marrow Examination. *Journal of Postgraduate Medical Institute* 2008; 22(3):1-8.
8. Jha A. Spectrum of Hematological Malignancies and Peripheral Cytopenias. *J. Nep. Health Rea. Cou.* 2013; 11(25):273-278.
9. Saeed MS, Jawhar NM. Bone marrow trephine in some hematological and non-hematological disorders. *Ann Coll Med.* 2010; 36(1&2):63-71.
10. Nigam RK, Malik R, Kotharia S, Gour D, et al. Spectrum of Diseases Diagnosed By Bone Marrow Examination In Central India. *J Evo Med Dent Sci.* 2014; 3(2):326-337.
11. Pudasaini S, Prasad KBR, Rauniyar SK, Shrestha R, Gautam K, Pathak R, Koirala S, Manandhar U, Shrestha B. "Interpretation of bone marrow aspiration in hematological disorder". *J of Pathology of Nepal* 2012; 2:309-312.
12. Singh I, Jain R, Gupta GN, Goyal PK. Epidemiological, etiological and hematological

studies on acquired aplastic anemia. Int J Pharm Res Bio Sci. 2014; 3(3):242-255.

13. Momani A, Rame Khasawneh, Abed R. Spectrum of Bone Marrow aspiration test results at Prince Rashid Hospital/Jordan; A 3 Year Experience. Int J Bio Med Res. 2012; 3(2):1648-1650.

14. Mahajan V, Kaushal V, Thakur S, Kaushik R. A comparative study of bone marrow aspiration and bone marrow biopsy in haematological and non haematological disorders- An institutional experience. J Ind Acad Clin Med. 2013; 14(2):133-135.

How to cite this article:

Singh I, Jain R, Gupta GN and Goyal PK: Evaluation of Bone Marrow for Hematological anomalies in Indian Pediatric and Adult Patients: A Single Tertiary Care Center Study. Int J Pharm Sci Res 2015; 6(4): 1584-89. doi: 10.13040/IJPSR.0975-8232.6(4).1584-89.

All © 2013 are reserved by International Journal of Pharmaceutical Sciences and Research. This Journal licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License.

This article can be downloaded to **ANDROID OS** based mobile. Scan QR Code using Code/Bar Scanner from your mobile. (Scanners are available on Google Playstore)